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By DJ Quinn

AUG

CGNE 69-4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	
Thompson, et al.	Examiner: P. Moody
Serial No. 07/762,762	Art Unit: 1804
Filed: SEPTEMBER 16, 1991	TRANSMITTAL FOR APPEAL BRIEF UNDER 37 C.F.R. § 1.192 AND AMENDMENT UNDER § 1.116(b)
For: PLANT DESATURASES - COMPOSITIONS AND USES	

Honorable Commissioner of
Patents and Trademarks
Washington, DC 20231

Dear Sirs:

Enclosed is a brief in support of an appeal to the Board of Patent Appeals and Interferences, submitted in triplicate. Applicants appeal the final decision of the Examiner in an Advisory Action dated April 7, 1994, wherein all pending claims in the above application were rejected.

Applicants enclose an amendment to the specification in an attempt to put the application into better form for appeal.

Applicants also enclose a check in the amount of $630.00 to cover an Extension of Time fee of $360.00, to extend the period for filing the brief from April 21, 1994 to July 21, 1994, and the fee for filing a brief in support of an appeal of $270.00. Please apply any charges not covered, or any credits, to Deposit Account No. 03-0173.

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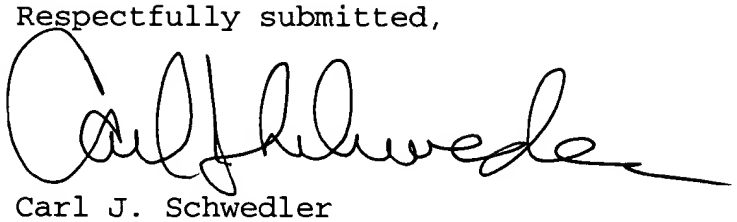
A duplicate copy of this letter is enclosed for accounting purposes.

Respectfully submitted,



Carl J. Schwedler
Reg. No. 36,924

CALGENE, INC.
1920 Fifth Street
Davis, CA 95616
(916) 753-6313

enclosure: Check in the amount of $630.00
Amendment under 37 C.F.R. §1.116(b)
Brief in support of appeal (in triplicate)

#270.00 -120 -Rq/84

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(Date of Deposit)

By DJ Owen

8/5/94

AUG CGNE-69-4

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the Application of	
Thompson, et al.	Examiner: P. Moody
Serial No. 07/762,762	Art Unit: 1804
Filed: September 16, 1991	APPEAL BRIEF UNDER 37 C.F.R. §1.192
For: PLANT DESATURASES - COMPOSITIONS AND USES	

Honorable Commissioner of
Patents and Trademarks
Washington, DC 20231

Dkt-3227

Dear Sirs:

Applicants submit this brief, in triplicate, in support of Applicants' Appeal to the Board of Patent Appeals and Interferences from the decision of the Examiner in a Final Office Action dated September 21, 1993, wherein all claims in the above application were rejected. The claims under appeal are found in the accompanying Appendix.

STATUS OF CLAIMS

Claims 18, 21, 26, 33, 35-36, 41, 68-71, 73-78 and 80-82 are pending in the application.

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STATUS OF AMENDMENTS

In the April 7, 1994, Advisory Action, it was indicated that amendments made in Applicants' response dated March 21, 1994, would be entered upon filing of an appeal.

Also in that Advisory Action the rejection of certain claims under §112, second paragraph for duplication was withdrawn in view of claims canceled, and the rejections of Claims 74, 79 and 81 were withdrawn in view of canceled or amended claims. Also withdrawn was the new matter objection regarding Figure 11, in view of the cancellation of this figure.

Applicants also submit an amendment herein to add a reference to a deposit of the antisense construct in the specification, namely construct pCGN3242. The amendment is made pursuant to 37 C.F.R. §1.116 to remove an issue for consideration on appeal.

SUMMARY OF THE INVENTION

Fatty acid modifying plant desaturases are enzymes which introduce double bonds into a fatty acid molecule through a desaturation reaction. One such reaction involves the desaturation of stearoyl-ACP (C18:0) to form oleoyl-ACP (C18:1), in a reaction catalyzed by a stearoyl-ACP desaturase, also often referred to as a "Δ-9 desaturase" in that it functions to add a double bond at the ninth carbon. Other double bonds may be added at the twelve position and 15

position carbons, through the action of Δ-12 desaturase and Δ-15 desaturase, respectively.

This invention provides the first evidence that the saturation levels of plant fatty acids can be modified by a method of growing a plant cell containing a recombinant construct which includes an encoding sequence to a plant desaturase. The specification provides encoding sequences to four separate plant desaturases, from such diverse plants as rapeseed (*Brassica campestris*), safflower (*Carthamus tinctorius*), castor bean (*Ricinus communis*) and jojoba (*Simmondsia chinensis*), and the means for obtaining other plant desaturase encoding sequences.

ISSUES

Issue 1

Are the claims incomplete for failing to recite an antisense orientation for the cDNA, and thereby fail to satisfy the requirements 35 U.S.C. §112, second paragraph?

Issue 2

Does the specification adequately describe the constructs and enable practice of the invention, and are the methods recited in the claims enabled within the meaning of 35 U.S.C. § 112, first paragraph?

Issue 3

In order to satisfy the requirements of 35 U.S.C. § 112, first paragraph, must the claims be limited in scope to methods of altering *Brassica* oil compositions utilizing constructs containing antisense *Brassica* desaturase cDNAs?

Issue 4

Are the claimed methods obvious under 35 U.S.C. § 103 over Kridl *et al.* taken with Knauf and Shewmaker *et al.*, and further in view of McKeon *et al.* and Weissman *et al.*?

GROUPING OF THE CLAIMS

Unless otherwise stated in the appropriate portions of the argument, all claims are to be considered as a single group for purposes of patentability under each basis for rejection.

ARGUMENT

Issue 1

The instant specification (1) exemplifies methods for modifying the fatty acid composition of plant cells by growing plant cells containing "sense constructs" (Example 9), and (2) exemplifies methods for modifying the fatty acid composition of plant cells by growing plant cells containing "antisense constructs" (Example 13). By "sense" and "antisense" is meant the orientation of the desaturase encoding sequence relative to the regulatory elements which

govern the transcription of RNA from the constructs. A "sense construct" will have a desaturase encoding sequence oriented such that the RNA transcribed from the construct will comprise the desaturase protein encoding sequence, or the "sense" strand of nucleic acid. An "antisense construct" has a desaturase encoding sequence oriented such that any RNA transcribed from that construct will comprise nucleic acid which is a mirror image to the encoding strand. There is no evidence of record to indicate that the inventors only regard their invention as comprising methods for antisense inhibition of desaturase. In fact, claims generic to sense and antisense methods were submitted with the application as filed.[1] Applicants have never been asked, nor have they ever volunteered or agreed, to restrict prosecution of this case to claims reciting a method of antisense inhibition.[2]

Additionally, Claims 35, 70, 74-75, 78 and 81-82 do recite an antisense limitation in the claimed method, so the rejection under §112, second paragraph, should not be applied to these claims.

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[1] For the purposes of § 112, second paragraph, it is presumed that the subject matter set forth in a claim is that which is regarded as the applicant's invention, in the absence of evidence to the contrary. *In re Miller*, 441 F. 2d 689, 692 (CCPA 1971). The only proper ground of rejection is "where some material submitted by applicant, other than his specification, shows that a claim does not correspond in scope with what he regards as his invention." *In re Conley*, 490 F. 2d 972, 976 (CCPA 1974).

[2] In an Office Action dated October 9, 1992, Claims 18, 21 and 26 were identified as a Group II invention, comprising claims generic to several species, including an expressed protein species (sense) and an enzyme inhibition species (antisense). Applicants elected the generic Group II claims as well as species claims directed to enzyme inhibition.

In light of the above, Applicants respectfully request that the 35 U.S.C. §112, second paragraph, rejection of these claims be reversed.

Issue 2

For the purpose of reducing issues for Appeal, Applicants amend the specification herewith to include a reference to the deposit of the antisense construct pCGN3242. The amendment to reference this deposit is not necessary to obviate this rejection (37 C.F.R. 1.802(c)), and is not submitted as an admission or acquiescence on the merits of this rejection. (See *Quad Environmental Technologies Corp. v. Union Sanitary District*, 20 U.S.P.Q. 1392 (Fed. Cir. 1991)).

The instant specification exemplifies methods for using plant desaturase encoding sequences in the modification of plant fatty acid compositions. The specification describes several desaturase sequences, plant regulatory sequences, sense and antisense constructs, plant transformation methods and concludes with an analysis of fatty acid compositions demonstrating that fatty acid modification was achieved, through methods using both the antisense and the sense constructs. The §112, first paragraph rejection should be overturned if for no other reason than this detailed description in the specification.

Additionally, it is well established that if one ordinarily skilled in the art can practice the claimed

invention without undue experimentation, combining the knowledge of the prior art with the disclosure of the specification, then the enablement requirement of §112 is satisfied. *Northern Telecom, Inc. v. Datapoint Corp.*, 908 F.2d 931, 943 (Fed. Cir. 1990). Furthermore, "[i]t is not fatal if some experimentation is needed, for the patent document is not intended to be a production specification." *Id.*

The allegation that the specification does not adequately describe constructs used in the invention, or the suggestion that one particular construct, pCGN3242, is essential to the claimed invention (see paragraph 3 of page 6 in the Final Office Action), ignores the reality of the advanced skill of the art in plant biotechnology at the time of this invention. The skilled artisan truly required nothing more than the desaturase sequences themselves to produce antisense or sense constructs for plant transformation, and the descriptions of successful fatty acid modifications in the specification provide the expectation of success to the skilled artisan to practice the claimed methods using such constructs.

However, with regard to antisense inhibition by such a construct, it is alleged that the specification is lacking as to teaching which portions "must be in the antisense orientation or what other elements must be included" (page 5 of the Final Office Action). The specification includes several desaturase sequences, exemplary sense and antisense

vectors, and techniques for plant transformation and analysis of the resulting plants. There simply are no other elements which must be included to achieve the stated end result of plant fatty acid modification.

As to the issue of necessary portions of antisense sequence, Applicants must merely enable the skilled artisan to reproduce these results. The instant specification exemplifies antisense inhibition. In any case, antisense inhibition of plant genes was a routine tool at the time of filing the present specification. This much is apparently conceded by the Patent Office in the Final Office Action, at page 9, wherein the Shewmaker *et al.* patent cited against the claims under §103 is summarized as teaching "the application of antisense for any gene in order to reduce expression of the message encoding the product of that gene" (page 11). The state of the art with regard to antisense inhibition is of record in this application and includes successes in modifying a number of basic biochemical processes in plants, including fruit ripening (Shewmaker *et al.*), flower color (antisense chalcone synthase; van der Krol *et al.*) and a photosynthetic enzyme (antisense of RuBisCo subunit (Rodermel *et al.*).

At the time of the invention the skilled artisan was not questioning what mystery "portions" of a plant desaturase encoding sequence should be included in an antisense construct. The skilled artisan only lacked the desaturase sequences and an answer to the question of whether fatty acid

compositions could be altered at all by antisense inhibition of the desaturase enzyme. Applicants provide both.

For all of the above reasons, reversal of the objection to the specification and rejection to the claims made under §112, first paragraph, is respectfully requested.

Issue 3

There is no basis for limiting the claims to methods of altering *Brassica* oil composition utilizing constructs containing antisense *Brassica* stearoyl-ACP desaturase cDNAs, as the specification clearly warrants claims which embrace modifications to plant cells through both sense and antisense methods, and utilizing any and all plant desaturases. To the extent the board agrees that particular limitations are required, the claims which recite a relevant limitation will be set out in the appropriate portion of the argument.[3]

Antisense Limitation

Methods for modifying fatty acid compositions using both antisense and sense desaturase sequence constructs are clearly enabled by the specification. A method using a napin promoter construct with sense desaturase is exemplified in the specification in Example 9, with results on page 86 demonstrating modified fatty acid contents of plant cells. Since the specification includes exemplified modifications to fatty acid and oil triglyceride compositions using both sense

[3] Claims 70, 75, 78 and 82 contain the limitations at issue and are not subject to the rejection forming the basis of Issue 3.

expression (Example 9) and antisense inhibition of the desaturase protein (Example 13), that aspect of this rejection limiting the claims to antisense inhibition is simply wrong, and should be reversed. Claims 35, 74 and 81 recite such a limitation, and should not in any case be rejected as lacking an antisense limitation.

Brassica Stearoyl-ACP Desaturase

Each of the four desaturase sequences disclosed in the instant specification encode a stearoyl-ACP desaturase. The four desaturases are sufficiently homologous to be identified from hybridization to other of the stearoyl-ACP desaturase encoding sequences. Furthermore, two of these desaturase encoding sequences are exemplified in the specification in modifications of the fatty acid composition of plant cells. In Example 9 the modification is accomplished by a method utilizing a construct comprising a sense encoding sequence to safflower desaturase.

As the specification describes four related stearoyl-ACP desaturases from diverse plant species, and exemplifies modifications of fatty acid compositions using both safflower desaturase cDNA constructs and *Brassica* constructs, the aspect of this rejection limiting the claims to methods utilizing *Brassica* stearoyl-ACP desaturase cDNAs should be reversed. Claims 68-69, 71 and 76-77 recite a method utilizing a stearoyl-ACP desaturase encoding sequence to modify the fatty acid composition of a plant cell.

Any and All Plant Desaturases

Claims 18, 21, 26, 33, 35-36, 41, 73-74, and 80-81 recite a limitation to fatty acid modifying plant desaturases. These claims do not embrace any and all plant desaturases, for other desaturases may exist which do not operate to modify fatty acid saturation levels.

The disclosure of the instant application represents the first demonstration of a successful modification of plant saturated fatty acid levels using a recombinant construct. In fact, Applicants results are truly the first demonstration that the fatty acid biosynthesis pathway in plants is amenable to manipulation through biotechnology at all. While each of the plant desaturases provided in the specification are stearoyl-ACP desaturases, other desaturases are known, such as are described on page 4 of the specification. It is reasonable to extrapolate from Applicants successes using stearoyl-ACP desaturases that alternative desaturases may be obtained and used successfully in the modification of plant fatty acid saturation levels.

More particularly, the specification teaches isolation and purification techniques for obtaining plant desaturase encoding sequences, and describes sequences from four separate plant species. From such a disclosure the skilled artisan would have an expectation of success in obtaining encoding sequences to other desaturases. This entitles Applicants to claim their invention such as to embrace methods utilizing fatty acid modifying plant desaturases.

Brassica Cells Limitation

The instant specification provides a first demonstration of the principal that saturated fatty acid levels of plant cells can be affected by a construct encoding a fatty acid desaturase. The fact that the fatty acid modifications described in the specification are exemplified in *Brassica* cells does not imply that other plant cells could not be similarly modified. "[T]o be enabling, the specification of a patent must teach those skilled in the art how to make and use the full scope of the claimed invention without 'undue experimentation.'... Nothing more than objective enablement is required, and therefore it is irrelevant whether this teaching is provided through broad terminology or illustrative examples." *In re Wright*, 999 F.2d 1557, 1561 (Fed. Cir. 1993).

Furthermore, it is well established in patent law that broad protection should be allowed for pioneer inventions. the court in *In re Hagen & Banks*, 559 F.2d 595 (CCPA 1977) stated:

> The PTO has not challenged the appellants' assertion that their 1953 application enabled those skilled in the art in 1953 to make and use "a solid polymer" as described in a claim. The appellants disclosed, as the only then-existing way to make such a polymer, a method of making the crystalline form. To say now that the appellants should have disclosed in 1953 an amorphous form (which did not exist until 1962) would be to impose an impossible burden on inventors and thus on the patent system. There cannot, in any effective patent system, be such a burden placed on the right to broad claims. To restrict the appellants to the crystalline form disclosed, under such circumstances, would be a

> poor way to stimulate invention. and particularly to encourage its early disclosure. To demand such restriction is merely to state a policy against broad protection for pioneer inventions, a policy both shortsighted and unsound from the standpoint of promoting progress in the useful arts, which is the constitutional purpose of the patent laws.

The Federal Circuit has also held that a liberal view of claim interpretation should be afforded a pioneer invention. *Texas Instruments v. United States International Trade Commission,* 846 F.2d 1369 (Fed. Cir. 1988).

There is no evidence of record to suggest that *Brassica* cells are critically different from other plant cells or somehow unique in their approach to desaturation of fatty acids. Rather, the record demonstrates that at the time of the invention the fatty acid metabolic pathway was known to be similar among diverse plant species (see Figure 2 of the Knauf reference, for example). Moreover, the four desaturase enzymes described in the specification, from four diverse plant species, are highly conserved.

In judging the enablement of the present invention, the specification must be accepted for the full range of enablement disclosed unless the Examiner can provide sufficient proof to doubt the accuracy of the disclosure. *In re Marzocchi*, 169 U.S.P.Q. 367 (CCPA 1971). As the understanding of the skilled artisan was quite advanced at the time of this invention, both as to plant transformation techniques and plant fatty acid metabolism, such a one would have had an expectation of success in using the claimed methods in other plant cells, once apprised by the instant

specification of the necessary encoding sequences and of Applicants' success in *Brassica*.

Therefore, limitation to a particular cell type is not warranted for these claims as they are directed to a method for modifying the fatty acid composition of a plant cell, and the teachings of the specification both enable its practice and provide the skilled artisan with an expectation of success for modifying the fatty acid composition of any plant cell by such a method.

Claims 69 and 77 recite a *Brassica* cells limitation, so even assuming that the claims should be limited in scope to *Brassica* cells, these claims should not be rejected on that basis.

In view of the above, Applicants are clearly entitled to the scope of protection in Claims 18, 21, 26, 33, 35-36, 41, 68-69, 71, 73-74, 76-77 and 80-81, and reversal of the 35 U.S.C. §112, first paragraph rejection to the claims is respectfully request. Claims 70, 75, 78 and 82 contain limitations to *Brassica* cells and *Brassica* cDNA in an antisense orientation, and are not subject to the Issue 3 basis of rejection.

Issue 4

The §103 rejection presumes that a desaturase encoding sequence for use in the claimed method is obvious from the teachings of the prior art. The teachings of the tertiary

references, McKeon *et al.* and Weissman *et al.*, are cited as rendering obvious such a plant desaturase encoding sequence.

Purified Desaturase Protein

McKeon *et al.* was initially cited by the Patent Office as providing a purified desaturase protein preparation. In a declaration submitted during prosecution, Dr. Thompson, an inventor, detailed problems with the desaturase protein preparation obtained using the method described in McKeon *et al.*, which are also described in the specification (*see*, specification, page 24, lines 10-19; also Examples 2 and 3).

As noted in Dr. Thompson's declaration, the contamination in the McKeon *et al.* preparation led Applicants to clone a cDNA to albumin, after undertaking amino acid sequencing and cloning procedures similar to those described in Weissman *et al.*, i.e., hybridization to a cDNA library using oligonucleotides derived from the amino acid sequence of the purportedly purified desaturase protein. After determining that they had cloned albumin, Applicants went back and further analyzed the desaturase preparation of McKeon *et al.*, and discovered that albumin protein constitutes about 50% more protein, on a mole percentage basis, than desaturase in this preparation. Section 103 provides that "[p]atentability shall not be negatived by the manner in which the invention was made."

The Advisory Action asserts, however, that "one of ordinary skill in the art would have used the gel slice to

obtain the protein sequence as a matter of routine". This is in apparent reference to the ~ 36 kDa band of protein visible in lane 9 of the polyacrylamide gel depicted in Figure 2 of McKeon *et al.*. The prior art does not, however, teach or suggest cutting this gel to produce a gel slice. It has also not been pointed out where in the prior art it is taught to routinely slice polyacrylamide gels.[4]

The only motivation to purify desaturase from the McKeon *et al.* preparation comes from Applicants, who first report the existence and the extent of the albumin contamination in the instant specification. It is inappropriate to use the invention as a template to piece together the teachings of the prior art. *In re Fritch*, 972 F. 2d 1260, 1266 (Fed. Cir. 1992) "It is impermissible ... simply to engage in a hindsight reconstruction of the claimed invention, using the applicant's structure as a template and selecting elements from references to fill the gaps." *In re Gorman*, 933 F. 2d 982, 987 (Fed. Cir. 1991). The idea of using a gel slice, or any other purification step, to further purify desaturase from the preparation of McKeon *et al.* is precisely such a hindsight reconstruction.

The prior art and the instant specification both teach methods for isolating or purifying protein from a polyacrylamide gel, and there are undoubtedly many other methods which could have been used to purify the desaturase preparation of McKeon *et al.*, had one known the desaturase

[4] Nor has this allegedly routine practice previously been cited in prosecution as forming part of the §103 rejection.

was contaminated and had one understood the nature of that contamination, but no such knowledge and no such understanding existed in the prior art. Obviousness "cannot be established by combining the teachings of the prior art to produce the claimed invention, absent some teaching or suggestion supporting the combination." *In re Fine*, 837 F. 2d 1071, 1075 (Fed. Cir. 1988) (quoting *ACS Hospital Systems, Inc. v. Montefiore Hospital*, 732 F. 2d 1572, 1577 (Fed. Cir. 1984). The Patent Office has improperly used the fact of an albumin contamination which is founded only in the instant specification as the motivation to combine a further purification step from the prior art. "That a technician, in hindsight, could combine elements known within the technology to produce the contested patent does not make the patent obvious to one skilled in the art...." *Symbol Technologies Inc. v. Opticon Inc.*, 17 U.S.P.Q. 2d 1737, 1746 (S.D.N.Y. 1990), *aff'd* 935 F.2d 1569 (Fed. Cir. 1991). That there existed a capability in the art to make a gel slice is not a substitute for some motivation in the art to make such a gel slice.

The gel depicted in McKeon *et al.* is a sizing gel run on samples of protein to estimate both the purity of the preparation and the size of the protein purified. There is only one visible band in the preparation run in lane 9 of the gel of McKeon *et al.*, and the preparation is characterized by the McKeon *et al.* reference as being nearly homogeneous. McKeon *et al.* teaches away, then, from the desirability of

further purification of the desaturase protein, and in fact reports that further attempts at purification caused a great loss of activity, such that further purification was discontinued (paragraph spanning 12142-12143).

The issue of whether a purification technique would have been practiced as a matter of routine regardless of the reported purity of a protein was addressed in a case decided in 1990. *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 13 USPQ2d 1737 (D. Mass, 1990). In *Amgen*, a Miyake *et al.* reference reported purification of EPO protein to apparent homogeneity. The Miyake *et al.* reference includes a Figure 5 which depicts an SDS polyacrylamide gel run on a sample of purportedly purified EPO protein, and which shows a single visible band of protein. The court in *Amgen* concluded that the prior art did not suggest the desirability of applying an extra purification step (RP-HPLC) to such a preparation, because the protein reported in Miyake *et al.* was already believed to be pure. *Id.* at 1784-1785.

The *Amgen* case was made of record by Applicants during prosecution of this case. In apparent response it was noted in the Advisory Action that the "purity of the gel slice" itself is not disputed. As noted above, there is no gel slice in the prior art. The issue is whether <u>any</u> motivation is present in the art to further purify the protein preparation taught by McKeon *et al.*.

It is the instant specification which teaches the contamination, and the instant specification which

establishes that amino acid sequence can be successfully obtained from desaturase protein, but only once the albumin contamination has been dealt with. "A patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified." *In re Sponnoble*, 405 F. 2d 578, 585 (CCPA 1969).

cDNA to Desaturase

Even assuming that McKeon *et al.* provided a purified desaturase protein, an issue remains as to whether Applicants' claimed methods would be obvious in light of such a purified desaturase protein.[5] In the §103 rejection, the Weissman *et al.* reference is characterized by the Patent Office as teaching that all one of ordinary skill in the art needed in order to obtain cDNA for any gene was a purified protein preparation. While Applicants dispute that McKeon *et al.* provides such a purified protein preparation, they also

[5] The restriction made in this case (dated October 9, 1992) grouped those claims reciting desaturase constructs (Group I) separately from claims to methods of modifying fatty acid compositions (Group II), as distinct and unobvious separate inventions. MPEP 802.01. Clearly, then, the claimed methods should be considered unobvious over a reference purporting only to describe a purified desaturase protein. Applicants also fail to understand the nature of whatever double patenting rejection was intended in the last few lines of the Advisory Action (at box marked "Other", wherein it is stated "however, upon review of 07-979461 & 07-615784 there appears to be double patenting over presently amended claims.") This appears to be contrary to the above noted restriction, in that all of the claims being prosecuted in the copending applications recite constructs or other inventions which have already been grouped in the instant case as distinct from the method claims.

dispute that Weissman *et al.* renders the nucleic acid sequence to a protein obvious simply given a purified preparation of that protein.

Applicants view of Weissman *et al.* is supported by a holding of the Federal Circuit Court of Appeals, which reviewed the teachings of the *Weissman et al.* reference in a decision handed down in 1993. *In re Bell*, 26 USPQ2d 1529. The issue of *In re Bell* was whether "the amino acid sequence of a protein in conjunction with a reference indicating a general method for cloning renders the gene *prima facie* obvious." *In re Bell* at 1531. The Patent and Trademark Office had argued that "in view of Weissman, a gene is rendered obvious once the amino acid sequence of its translated protein is known." *Id.* at 1532.

The Federal Circuit held in that case that a rejection of an invention based on Weissman *et al.* and a primary reference showing the amino acid sequence amounts to a rejection based on the sequence of the primary reference alone. *Id.* at 1531. Under the Federal Circuit's reasoning in *In re Bell*, the Weissman *et al.* teaching did not render the nucleic acid sequence of the protein obvious, even though the amino acid sequence was known. Applicants note particularly the holding that the claimed nucleic acid sequence would not have been obvious because an amino acid sequence is only a suggestion of the vast number of possible DNA sequences which could encode for that amino acid sequence. *Id.* at 1531.

Under the present fact case the desaturase cDNA is even less obvious than was the situation for the cDNA encoding sequence in *In re Bell*. In *In re Bell* the primary reference provided the amino acid sequence for the protein, while McKeon *et al.* does not provide an amino acid sequence for the desaturase protein, but only purports to disclose a purified desaturase protein preparation, which, even assuming flawless execution with no complications in practicing the method of Weissman *et al.*, is several steps removed from an amino acid sequence.

Expectation of Success

Even assuming that a cDNA to desaturase were available there was no expectation of success in modifying plant fatty acids by such a method at the time of this invention. A proper analysis for obviousness must approach the claimed invention as a whole. *Kimberly-Clark Corp. v. Johnson & Johnson,* 745 F,.2d 1437, 1448 (Fed. Cir. 1984). In the instant case the claims recite a method utilizing a recombinant construct.

To render an invention obvious the prior art must not only suggest the invention and suggest that it is reasonably likely to succeed, but further "both the suggestion and the expectation of success must be founded in the prior art, not in the applicants disclosure." *In re Dow Chemical*, 837 F.2d 469, 472 (Fed. Cir. 1988). However, it is Applicants' disclosure which provides the methods to modify plant fatty

acid compositions, the desaturase encoding sequence for making the constructs used in the methods, and the assurance that such methods will work. Absent some evidence that expressed or antisensed desaturase would have any affect on desaturated fatty acid compositions, the skilled artisan would have at best been able to speculate as to the possibilities. The prior art clearly contains neither a teaching of a specific method to be used nor a demonstration of a reasonable expectation of success for any particular approach.

The primary and secondary references have been cited, however, as providing everything necessary, other than the desaturase encoding sequences, to modify fatty acid compositions by the claimed method. Kridl *et al.* describes seed specific expression of an ACP gene during lipid development. There is no disclosure in Kridl *et al.* of a recombinant plant fatty acid modifying cDNA construct, nor does Kridl *et al.* provide any expectation of success for a method of modifying fatty acid composition using a desaturase construct.

The Knauf secondary reference is a review which discusses several potential targets for research, such as increasing oil production and altering fatty acid compositions, but which contains no suggestion of a specific fatty acid synthesis gene encoding sequence or a specific construct. Thus, while Knauf may have provided a motivation to attempt to prepare fatty acid synthesis gene constructs

for the purpose of altering fatty acids in plant cells, it provides no means for accomplishing this goal and no basis for predicting success for any particular approach.

Shewmaker *et al.* teaches the use of an antisense cDNA construct to regulate a plant gene. The gene exemplified in Shewmaker *et al.* is not a fatty acid synthesis gene, and Shewmaker *et al.* reports no result which would give the skilled artisan reason to expect that similar success should be expected in modifying a fatty acid synthesis gene.

These references at best render the claimed invention "obvious to try".

> The admonition that "obvious to try" is not the standard under §103 has been directed mainly at two kinds of error. In some cases, [w]hat would have been "obvious to try" would have been to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful result, where the prior art gave no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful. In others, what was "obvious to try" was to explore a new technology or a general approach that seemed to be a promising field of experimentation, where the prior art gave only general guidance as to the particular form of the claimed invention or how to achieve it.

In re O'Farrell 7 U.S.P.Q. 2d at 1681 (Fed. Cir. 1988).

The recently released decision of the Board of Patent Appeals and Interferences concerned a similar 35 U.S.C. § 103 rejection as is presented here as Issue 4. *Ex parte Maizel* 27 U.S.P.Q. 2d 1662 (1993). As summarized by the Board in the *Maizel* case, it was the Examiner's position that a description of the usefulness of the subject protein (BCGF),

and the knowledge of the existence of that protein in the art, would have motivated one skilled in the art to:

> (1) isolate the protein, (2) sequence the protein, (3) construct synthetic DNA probes from the proteins, (4) utilize the probes to isolate messenger RNA, (5) synthesize a cDNA, and (6) produce additional protein.

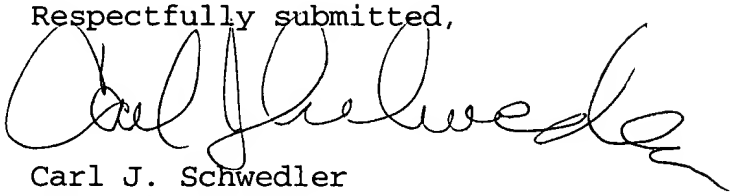
Maizel at 1688.

In reversing the obviousness rejection of *Maizel*, the Board stated that "the examiner's position reflects the 'obvious to try' approach of the 'armchair chemist'" *Id.* at 1168.

At the time of this invention the skilled artisan would have viewed the desaturase enzyme as only one among many fatty acid synthesis pathway genes which might be tried in an attempt to modify the fatty acid composition of a plant cell. Setting aside for the sake of argument the fact that the encoding sequence to desaturase was unknown at the time of this invention, the cited references provided only a suggestion to try using such a sequence in a method such as is claimed. No one had previously altered the expression of a fatty acid pathway gene to achieve a modified fatty acid composition phenotype. What was "obvious to try" was only an exploration of biotechnology in the area of fatty acid modification. The prior art may have pointed to this as a promising field of experimentation, but it provided only general guidance, at best, as to the particular form of the invention, and failed to provide a desaturase sequence and therefore could not detail how the invention might be achieved.

For all of the above reasons, reversal by Board of Patent Appeals and Interferences of the 35 U.S.C. §103 rejection of the claims is respectfully requested.

Respectfully submitted,



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APPENDIX

18. A method of modifying the fatty acid composition of a plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a fatty acid modifying plant desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

21. The method of Claim 18 wherein said regulatory elements function preferentially in plant seed cells.

26. The method of Claim 18 wherein said plant host cell is selected from the group consisting of rapeseed, sunflower, castor, cotton, *Cuphea,* peanut, soybean, oil palm and corn.

33. A method of modifying the fatty acid composition of oil triglycerides in an oil producing plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent

cell thereof, said construct encoding a fatty acid modifying plant desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

35. The method of Claim 33 further comprising the inhibition of endogenous plant desaturase.

36. The method of Claim 33 wherein said regulatory elements function preferentially in plant seed cells.

41. The method of Claim 33 wherein said plant host cell is selected from the group consisting of rapeseed, sunflower, castor, cotton, *Cuphea*, peanut, soybean, oil palm and corn.

68. A method of modifying the fatty acid composition of a plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a plant stearoyl-ACP desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

69. The method of Claim 68 wherein said plant host cell is a *Brassica* cell.

70. The method of Claim 69 wherein said construct encodes a *Brassica* stearoyl-ACP desaturase in an antisense orientation with respect to said regulatory elements.

71. The method of Claim 68 wherein said host cell is from an oil producing plant.

73. A method of modifying the fatty acid composition of a plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a plant desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the expression of said desaturase, wherein at least one of said fatty acid modifying plant desaturase and said regulatory elements is heterologous to said plant host cell.

74. A method of modifying the fatty acid composition of a plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a plant host cell having a recombinant DNA

construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a fatty acid modifying plant desaturase derived from said plant host cell under the control of, and in an antisense orientation with respect to, regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

75. A method of modifying the fatty acid composition of a *Brassica* cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a *Brassica* cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a *Brassica* stearoyl-ACP desaturase under the control of, and in an antisense orientation with respect to, regulatory elements preferentially functional in plant seed under conditions which will promote the activity of said regulatory elements.

76. A method of modifying the fatty acid composition of oil triglycerides in an oil producing plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a plant stearoyl-ACP

desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

77. The method of Claim 76 wherein said plant host cell is a *Brassica* cell.

78. The method of Claim 77 wherein said construct encodes a *Brassica* stearoyl-ACP desaturase in an antisense orientation with respect to said regulatory elements.

80. A method of modifying the fatty acid composition of oil triglycerides in an oil producing plant host cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a host plant cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a plant desaturase under the control of regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the expression of said desaturase, wherein at least one of said fatty acid modifying plant desaturase and said regulatory elements is heterologous to said plant host cell.

81. A method of modifying the fatty acid composition of oil triglycerides in an oil producing plant host cell from a

given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a plant host cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a fatty acid modifying plant desaturase derived from said plant host cell under the control of, and in an antisense orientation with respect to, regulatory elements functional in said plant cell during lipid accumulation under conditions which will promote the activity of said regulatory elements.

82. A method of modifying the fatty acid composition of oil triglycerides in a *Brassica* cell from a given weight percentage of saturated fatty acids to a different weight percentage of saturated fatty acids comprising

growing a *Brassica* cell having a recombinant DNA construct integrated into the genome of said cell or a parent cell thereof, said construct encoding a *Brassica* stearoyl-ACP desaturase under the control of, and in an antisense orientation with respect to, regulatory elements preferentially functional in plant seed under conditions which will promote the activity of said regulatory elements.